UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,422	09/17/2003	Guy A. Rouleau	GOUD:023USD3	3964

7590 04/27/2007

Michael R. Krawzsenek
Fulbright & Jaworski L.L.P.
Suite 2400
600 Congress Avenue
Austin, TX 78701

EXAMINER	
KOLKER, DANIEL E	
ART UNIT	**PAPER NUMBER**
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,422	ROULEAU ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-28* is/are pending in the application.

4a) Of the above claim(s) *28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *14-28* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/16/06, 1/29/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 29 January 2007 have been entered. Claims 1 – 13 are canceled; claims 23 – 28 are new. Claims 14 – 28 are pending.

Election/Restrictions

2. Newly submitted claim 28 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claim is drawn to SEQ ID NOs: 69 – 98, which were not elected in the reply filed 1 June 2006. In that reply, applicant elected to prosecute the invention of SEQ ID NO:65. In the office action mailed 21 August 2006, the examiner explained why the inventions of SEQ ID NOs: 69 – 98 constituted patentably distinct inventions, and why it would be burdensome to search and consider all those inventions along with the elected invention (SEQ ID NO:65). The examiner objected to claims which recited non-elected subject matter, and applicant has since canceled the non-elected subject matter from claim 15, but has also added new claim 28 drawn solely to that non-elected subject matter.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 28 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 14 – 27 are under examination.

Information Disclosure Statement

3. The information disclosure statement filed 16 October 2006 has been considered.

Applicant is advised that reference C77, cited on the IDS filed 16 October 2006, has been crossed off because it is duplicative. Note the reference was cited by the examiner on form 892 mailed with the office action of 21 August 2006. Thus the reference would appear on the face of a patent, should one issue from this application.

The IDS filed 29 January 2007 has been considered.

Entry C79 has been amended by the examiner to indicate that only a single page has been received, as opposed to 774 pages as written by applicant. The examiner is unable to determine the contents of the book referred to in the citation as it has not been submitted. Should applicant desire particular articles or chapters from the book to be considered by the examiner, applicant may of course submit them.

Entry C81, entitled "BLAST result" has been crossed off the IDS. A single sheet was submitted indicating that two sequences were compared and that no significant similarity was found. A handwritten note on the page is difficult to read. It is unclear whether the sequences compared were SEQ ID NO:12 and 13, or whether they were SEQ ID NO:72 and 73. Furthermore, the submitted document does not indicate the actual sequences that were submitted to the BLAST website, nor does it indicate when those sequences were published, nor who submitted them. The examiner is thus unable to determine what comparison was performed. Finally, as neither SEQ ID NO:12, 13, 72, or 73 is being claimed herein, it is not immediately obvious how the comparison is germane to patentability or examination. Should applicant desire particular accession numbers of particular databases be considered by the examiner, applicant may of course submit them.

Withdrawn Rejections and Objections

4. The following rejections and objections set forth in the previous office action are withdrawn:

A. The objection to claims 14 – 16 is withdrawn in light of the amendments which cancel non-elected subject matter.

B. The rejection of claims 20 – 22 under 35 USC 101 is withdrawn in light of the amendments. The claims no longer encompass non-statutory subject matter as they are directed to isolated cells only.

Maintained Rejections and Objections

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 – 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid sequence of SEQ ID NO:65, or for those specific mutations set forth in claims 25 – 27, does not reasonably provide enablement for all complements as broadly set forth in claim 14, or for all fragments or variants encompassed by claims 14 – 16. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is maintained with respect to claims 14 – 22 and extended to new claims 23 – 28 as explained below. Applicant is referred to the office action mailed 21 August 2006 for a more complete description of why claims that encompass fragments, derivatives, and allelic variants are not completely enabled. Briefly, the claims are sufficiently broad that they do not require any particular structural element to be present. Claims to products which are "allelic variants" of disclosed sequences cannot be made by the skilled artisan, because the specification does not disclose to the artisan what the structure of the full scope of those variants is. While certain variants are disclosed at p. 52 of the specification, what is actually enabled by the specification is relatively narrow, whereas what is claimed is very broad, in that it encompasses any allelic variant, including those not yet disclosed. The specification does not show which regions are common to all allelic variants, nor does it disclose any particular required degree of identity to a disclosed sequence. Furthermore, fragments and functional derivatives which retain "a biological function of an alpha subunit of a sodium channel", as recited in claims 15 – 16 are not reasonably enabled over their full scope. While certain biological activities are defined in the specification, the definition of biological activity set forth on p. 19 line 20 of the specification is not limited to any particular function. The definition is quite clearly inclusive, but not limiting. Thus the broadest reasonable interpretation of "biological activity" includes the ability to raise antibodies, in the case of proteins, or even the ability to modulate osmotic pressure across a semipermeable membrane, a biological function which can be provided by any molecule of sufficient size. The specification does not set forth how to use all the molecules within the scope of the claims, as it only discusses nucleic acids which encode sodium channels.

Additionally, claim 14 now encompasses any complement of SEQ ID NO:65, no matter the size. There is no requirement that "a complement" as claimed be able to have any function on its own, nor is there any requirement that the claimed nucleic acid molecules encode any particular amino acid sequence themselves. Thus the broadest reasonable interpretation of claim 14, part (b), includes nucleic acids which are complementary over very short stretches of SEQ ID NO:65. The specification does not teach the public how to use these complements. If applicant intends to only claim those molecules which are complementary to SEQ ID NO:65 over its entire length, it is recommended that applicant amend the claims to recite language

such as "a full-length complement of SEQ ID NO:65", provided there is sufficient basis in the specification.

Thus given the breadth of the claims, the lack of disclosure in the specification commensurate with this broad scope, and the fact that the claims encompass an unreasonably large number of products which the specification does not disclose how to use, the skilled artisan would essentially have to discover how to use these products by himself. Given the lack of adequate guidance commensurate in scope with what is claimed, the artisan would have to resort to an undue amount of experimentation in order to determine how to make and how to use the full scope of the products encompassed by these claims.

Applicant argues, on p. 9 of the remarks, that the state of the art has progressed since the publication by Rudinger 30 years ago. The examiner is well aware that technical improvements in methods of making mutant proteins have developed, but the basic thrust of the article, and the particular passages cited, has not in fact changed. Inferring protein shape and function from amino acid sequence changes remains a very difficult problem that is full of unpredictability. See the attached article by Honig (October 1999. Journal of Molecular Biologiy 293:283-293), published about two months before the date the provisional application was filed in this case. Note that Honig teaches that despite technical progress since he began studying the problem of protein folding in 1970, considerable work remains to be done to be able to predict a protein's shape, and therefore its structure, once an amino acid sequence is known. See p. 289 – 290 for a discussion of the problems and challenges that remain in this field. While applicant stated that there has been progress since Rudinger was published, there is no evidence of record that protein prediction is easy or routine, or that it has been reduced to practice for the proteins encoded by the claimed nucleic acids.

6. Claims 14 – 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

This rejection is maintained with respect to claims 14 – 22 for the reasons of record and extended to newly-added claims 23 – 27 as they all depend, either directly or ultimately, from claim 14. Briefly, while the specification does disclose a very few allelic variants, the genus of

allelic variants as a whole cannot reasonably be considered to be described. There is no identification of what structural elements are common to all variants, nor is there any indication as to which nucleic acids can be changed between said variants. Similarly, there is no description of what constitutes a fragment or functional derivative, as recited in claims 15 – 16. The specification does not disclose to the artisan which regions of SEQ ID NO:65 must be maintained such that the resulting protein has "a biological function of an alpha subunit of a sodium channel" as recited in claims 15 – 16. The skilled artisan cannot visualize the genus of sequences or chemical compounds claimed, because the specification does not describe them.

Furthermore new claim 24 encompasses any and all nucleic acids within the scope of claim 14 which are "associated with an increased susceptibility to idiopathic generalized epilepsy". The specification points out allelic variants within this broad genus, but does not indicate which structural elements are common to all members of the genus. There is no disclosure of the length or sequence identity compared to SEQ ID NO:65 which is required for the generic variant. The specification fails to disclose the full genus, and the skilled artisan could not determine what shape, structure, or sequence these nucleic acids or their encoded proteins have. The specification does not disclose to the public which particular variants are associated with all forms of idiopathic generalized epilepsy. As such, the full scope of the genus of claims 14 and 24 is not supported by the specification.

Applicant argues, on p. 10 of the remarks, that claim 14 is limited to nucleic acids at least 95% identical to SEQ ID NO:65. This may be applicant's intent, but the broadest reasonable interpretation of claim 14 includes any nucleic acid, independent of length, that is complementary to any section of SEQ ID NO:65. Furthermore, claim 15 encompasses any fragment of SEQ ID NO:65. While claim 15 depends from claim 14, since the products of claim 14 are not limited by any particular length, neither are those of dependent claims. Clearly the full genus of fragments, functional derivatives, allelic variants, and complements has not been described in the specification.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14 – 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Clare et al. (Conference on Molecular and Functional Diversity of Ion Channels and Receptors, New York NY May 14 – 17, 1998, published as Annals of the New York Academy of Sciences 1999. 868:80-83).

This rejection stands with respect to claims 14 – 22 and is extended to new claims 23 – 24 for the reasons of record and as explained below.

Applicant indicates he does not agree with the examiner's characterization of the reference by Clare as a printed publication that qualifies as prior art under 35 USC 102(b). However, applicant did not present any particular evidence that the reference is anything but a meeting paper. In contrast, the examiner provided evidence that this was a printed, as opposed to oral, publication presented at the meeting. See office action mailed 21 August 2006, p. 8, as well as the table of contents for Annals of the NY Academy of Science, mailed with that office action, which distinguished between "Poster Papers" and oral presentations. Thus in the absence of evidence as to why the reference is not in fact a printed publication as defined by § 102(b), the examiner is maintaining the position that it is such a reference.

Applicant and the examiner are in agreement that the reference by Clare discloses a nucleic acid which is reported to by a type III sodium channel. The examiner indicated that the reference discloses this nucleic acid is 9.5 kb (see Figure 2). The examiner and applicant are in agreement that the reference does not disclose the actual sequence of this nucleic acid. The disagreement as to whether or not the reference is anticipatory appears to be as to whether or not this nucleic acid, disclosed more than a year before applicant filed for a patent in this country, is inherently the same as the nucleic acid of SEQ ID NO:65 as recited in claim 14 for example.

Applicant argues, on pp. 10 – 11 of the remarks, that "for a reference to anticipate based on inherency, the inherency must be '**certain**'." (emphasis in original). Applicant cites In re Oelrich and Ex parte Cyba in support of this argument. While the cases cited do state that what is asserted to be inherent must necessarily be present, several other cases as well as MPEP § 2112, support the examiner's contention that the burden is on applicant to distinguish what is now claimed from the product disclosed in the prior art. See for example *In re Best* 195 USPQ 430, 433 (CCPA 1977), where the court stated:

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, [4] the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. See In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Here, the product disclosed in the prior art is a nucleic acid that encodes a type III sodium channel and is isolated from human brain (see Clare, title). Instant SEQ ID NO:65 is "the cDNA sequence of the adult form of SCN3a" (specification, p. 27, lines 24 – 25). "SCNA" means sodium channel (specification, p. 3 lines 18 – 19). The only difference between "SCN3A" as defined in the specification and "Type III Na+ channel" as referred to by Clare appears to be the choice of Arabic numbers in the former and Roman numerals in the latter. Both are type 3 (or III) sodium channels, both are from humans. Thus as in *Best*, the product now claimed appears to be identical to that in the prior art. Because the PTO cannot manufacture and compare the prior art product and applicant's claimed invention, the burden is on applicant to distinguish the claimed invention from the prior art product.

MPEP § 2112 IV states that the examiner must provide a scientific rationale tending to show inherency. In the office action mailed 21 August 2006, the examiner did just that; he pointed out that both the prior art and the claimed invention are nucleic acids encoding sodium channels. The reference by Clare provides evidence that the product encodes a sodium channel; see for example Clare, Figure 1 which shows the channel is voltage dependent and tetrodotoxin (TTX) sensitive. The examiner also indicated that the prior art nucleic acid is reported to be about 9.5 kb in size, as indicated by the Northern blot (Clare, Figure 2); note the nucleic acid is isolated on the blot and the ~ character in front of 9.5 kb indicates it is an approximate size. Applicant's SEQ ID NO:65 is 9112 nucleotides, or 9.1 kb. Thus the examiner provided a clear scientific rationale that the products are identical: they have the same name, they were isolated from the same tissue, are approximately the same size, and both encode sodium channels. Alternatively, the prior art product comprises instant SEQ ID NO:65, as the prior art may be slightly larger (~9.5 kb vs. 9.1 kb)

MPEP § 2112 V states that "once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the examiner presents evidence or

reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference" (see heading). Applicant argues that the product now claimed is different from that in Clare. In support of the argument, applicant sets forth the following evidence:

1) Clare detects two bands, one being ~9.5 kb and the other being ~7.5 kb. The 7.5 kb band is present in skeletal muscle, whereas SCN3A from Thimmapaya et al. (2005) is not present in skeletal muscle

2) The probe from Clare detects another nucleic acid, which applicant speculates may be SCN4A.

3) The $V_{1/2}$ for the channel encoded by Clare's nucleic acid is 58 mV, whereas the $V_{1/2}$ for SCN3A from Chen et al. (2000) is slightly higher (69 mV).

Each of the above points will be addressed in turn.

With respect to 1), whether or not the probe used by Clare either detects multiple bands or detects a product in skeletal muscle is not germane. The product at 9.5 kb, which is highly expressed in brain and isolated on the Northern blot, is the one that is patently indistinguishable from the nucleic acid of SEQ ID NO:65. Although the probe used by Clare does in fact detect more than one band, the probe is not identical to the cDNA that encodes the type III sodium channel. In fact, Clare et al. are careful to point out that the entire cDNA was not used as a probe; only a portion from the 5' untranslated region was used (p. 83, first complete paragraph). The smaller (7.5 kb) band is hypothesized to be a splice variant but whether or not it is such a variant is immaterial as to the identity of the full-length cDNA which encodes a functional sodium channel or of the 9.5 kb band.

With respect to 2), as was stated in the previous paragraph, whether or not the probe detects an additional nucleic acid is not relevant. The probe is not the full-length cDNA. It is from the 5' UTR (see Clare p. 83). The full-length cDNA, which encodes a functional sodium channel and the 9.5 kb band isolated on the Northern blot are both indistinguishable from the nucleic acid now claimed. Thus even if the 7.5 kb band is SCN4A as applicant argues, the prior art reference by Clare still anticipates the claimed invention.

With respect to 3), the differences appear to be slight (58 vs 69 mV) and may be the result of re-calculation of data. Note that the data depicted as Figure 1 in Clare et al. appear to be identical to those set forth in Figure 5 of Chen (2000. European Journal of Neuroscience 12:4281-4289, cited in remarks filed 29 January 2007. Note that in each case the error bars are small between –120mV and –80 mV, are relatively large from –60mV to –40mV, and are small

again at –10mV. Further in each case n=4 (see figure legends). The data appear to be the same, only the calculations differ. Thus is applicant is attempting to show that the data depicted in Chen (2000) are the true SCN3A data differences from those results are evidence of a different protein encoded by a different nucleic acid, the data are not convincing.

The examiner notes that applicant has attempted to distinguish the prior art product from Clare from those disclosed in Chen and in Thimmapaya, but has not provided evidence to distinguish the nucleic acid now claimed from Clare. Furthermore, as Clare teaches double-stranded DNA (i.e., cDNA which is double-stranded) the reference is also on point to element (b) of claim 14, which is not limited to full-length complements of SEQ ID NO:65 but merely requires the presence of "a complement" of any length.

For the reasons above and previously made of record, the rejection of claims 14 – 22 over Clare stands. Claim 23 is rejected as the nucleic acid encodes a sodium channel which has sodium channel function, as shown by the voltage-sensitive TTX-dependent evidence in Clare Figure 1. Claim 24 is rejected as it depends from rejected claim 14 and requires no additional structural limitations or features.

8. Claims 14 – 19 and 23 – 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Lu (1998. Journal of Molecular Neuroscience 10(1):67-70, of record).

This rejection stands for the reasons of record with respect to claims 14 – 19 and is extended to claims 23 – 24 as explained herein. Briefly, Lu teaches three cDNA clones, each of which is a part of the SCN3A nucleic acid. The examiner concedes that none of these clones themselves or even when overlapped, is at least 95% identical to instant SEQ ID NO:65 as argued by applicant. However, the scope of the claims is not limited to nucleic acids at least 95% identical to SEQ ID NO:65. Claim 14 includes any complement, independent of the length. The nucleic acids from Lu are double-stranded and thus include complements, anticipating claim 14. Claim 15 depends from claim 14 and also includes fragments. As the nucleic acids from Lu are fragments, they meet the structural limitations of claim 15. The nucleic acids encode fragments of proteins, and thus would necessarily have "biological activity" including the ability to raise antibodies. Claim 16 includes nucleic acids which encode "functional derivative[s]" of SEQ ID NO:67; as the nucleic acids encode truncated forms of the proteins, are biologically active, and can be derived from SEQ ID NO:67. Claims 17 – 19 are rejected as the reference by Lu teaches the nucleic acids in vectors.

Rejections and Objections Necessitated by Amendment

Claim Objections

9. Claim 15 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 15 broadens, rather than narrows, the scope of claim 14. Claim 14 is limited to SEQ ID NO:65, a nucleic acid complementary thereto, a nucleic acid at least 95% identical to either of those. However claim 15 includes sequences comprising *fragments* of SEQ ID NO:65, thereby broadening the scope of the claim.

Claim Rejections - 35 USC § 112

10. Claims 25 – 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant states, on p. 7 of the remarks, that support for newly-added claims 25 – 27 can be found at pp. 53 – 54 of the specification and Figure 7. The examiner is able to find disclosure of a deletion mutant at amino acid residue 43 of SCN3A protein, but not for any and all mutations at nucleic acid position 759 – 761 of SEQ ID NO:65. It is not immediately obvious that bases 759 – 761 encode amino acid residue 43. Even if they do, at best this provides support for deletion of these three nucleotides, but not for all mutations at these three sites. The specification discloses a G-to-A mutation in the nucleotides encoding residue 1035. It is not immediately obvious that nucleotide 3735 of SEQ ID NO:65 is this G. Even if it is, at best this provides support for a G-to-A mutation here, not for any and all mutations at this position. Additionally, the examiner is unable to find disclosure of purified nucleic acids with more than one mutation in SEQ ID NO:65, i.e. claim 25, part(c). Thus claim 25 constitutes new matter for this reason as well.

Should applicant disagree with the examiner's determination, applicant should point out those particular places in Figure 7 or in pages 54 – 55 which disclose the subject matter now claimed. Particularly, applicant should point out where each of the mutations is disclosed, as

well as where nucleic acids comprising "any combination of" said mutations, as recited in claim 25 part(c), is disclosed.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15 and 23 – 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is indefinite because it is drawn to nucleic acids and fragments thereof, but require that the nucleic acids have "a biological function of an alpha subunit of a sodium channel." Sodium channels are proteins, which are distinct from nucleic acids. It is unclear how the nucleic acid is to have the biological properties of a protein. Furthermore claim 15 is confusing as it states "said alpha subunit comprises a nucleic acid sequence...", but a sodium channel subunit, which is a protein, cannot comprise a nucleic acid sequence.

The term "is associated with" in claim 24 is a relative term which renders the claim indefinite. The term "is associated with" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The skilled artisan could not determine which nucleic acids are within the scope of the claim, as it is unclear what it means for the nucleic acid to be "associated with" the increased susceptibility. This aspect of the rejection might be overcome if the language were changed to "wherein the presence of the nucleic acid indicates the subject has an increased risk of idiopathic generalized epilepsy." However, applicant should ensure that any amendments to clarify the scope of the claims are fully supported in the disclosure as originally filed in order to avoid a rejection for recitation of new matter.

Conclusion

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DK

Daniel E. Kolker, Ph.D.
April 19, 2007

RCH

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER